

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
06 September 2024 (06.09.2024)



(10) International Publication Number
WO 2024/182749 A1

(51) International Patent Classification:

C07H 21/02 (2006.01) C12N 15/113 (2010.01)
C07H 21/04 (2006.01) C07H 21/00 (2006.01)
C12N 15/11 (2006.01)

(21) International Application Number:

PCT/US2024/018169

(22) International Filing Date:

01 March 2024 (01.03.2024)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/487,823	01 March 2023 (01.03.2023)	US
63/491,720	22 March 2023 (22.03.2023)	US
63/581,614	08 September 2023 (08.09.2023)	US
63/585,133	25 September 2023 (25.09.2023)	US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

(54) Title: DOUBLE STRANDED OLIGONUCLEOTIDE COMPOSITIONS FOR RNA INTERFERENCE AND METHODS RELATING THERETO

(57) Abstract: The present disclosure provides double stranded oligonucleotides, compositions, and methods relating thereto. The present disclosure encompasses the recognition that structural elements of double stranded oligonucleotides, such as base sequence, chemical modifications (e.g., modifications of sugar, base, and/or internucleotidic linkages) or patterns thereof, and/or stereochemistry (e.g., stereochemistry of backbone chiral centers (chiral internucleotidic linkages), and/or patterns thereof, can have significant impact on oligonucleotide properties and activities, e.g., RNA interference (RNAi) activity, Ago2 loading, thermal stability, in vivo stability, delivery to tissues and into cells, etc. The present disclosure also provides methods for treatment of diseases, e.g., hepatic diseases, central nervous system (CNS) diseases, etc., using provided double stranded oligonucleotide compositions, for example, in RNA interference.



WO 2024/182749 A1

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Published:

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*